SUPPORT FOR THE AMENDMENTS

By the present amendment, Claims 134, 145, 150, 176 and 177 have been amended to either reflect that the vaccinating compositions inhibit parasitemia in vivo in a host infected with the *Plasmodium* parasite or to correct a dependency. Claims 151 to 153 have been amended to reflect that the fragments consist of the respective concatenation of amino acids. The amendments to the claims are supported by the specification and the original claims. Accordingly, no new matter is believed to have been added to the present application by the amendments submitted above.

REMARKS

Claims 134, 139-142, 145, 148-155, 157, 158, 160, 161, 163, 164 and 166-177 are pending. Favorable reconsideration is respectfully requested.

Claim 150 has been rejected under 35 U.S.C. § 112, second paragraph as being indefinite. This rejection is believed to be moot, since the claim has been amended to depend from a pending claim. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 153, 169, 172 and 175 have been rejected under 35 U.S.C. § 103(a) over Longacre (1995) in view of Longacre et al (1994). For the following reasons, this rejection is respectfully traversed.

Longacre (1995) disclose the C-terminal sequence of the *Plasmodium cynomolgi* merozoite surface protein 1 (MSP-1) and its homologs with other *Plasmodium* species. As set forth in Figure 1 of this reference, a 1200 bp was amplified and cloned into the pVLSV200 plasmid and the new plasmid formed is pVLSV200C42. Thus, for the DNA sequence analysis the MSP-1 p42 was used. Thus this reference does not disclose or suggest a recombinant protein having a 19 kilodalton C-terminal MSP-1 protein of *Plasmodium cynomolgi* consisting of an amino acid sequence from Lys276 to Ser380 as shown in SEQ ID NO: 11.

Also, further reference to the cloning of the C-terminal is the sentence bridging pages 106-107 where the following is stated:

> ...to test the potential of the C-terminal region of MSP-1 as a vaccine for *P. vivax* malaria we have cloned and sequences the corresponding portion of the *P. cynomolgi* ceylonesis MSP-1 gene and compared its primary structure with the same regions of MSP-1 from other *Plasmodium* species.

Thus the purpose of Longacre (1995) was merely sequence comparison and not producing recombinant proteins that can inhibit parasitemia.

The Examiner has taken the position that Longacre 1995 "teaches the cloning of the *P. cynomolgi* MSP-1 C-terminal fragments of the protein and specifically teaches the use of a recombinant baculovirus for expression of the *P. cynomolgi* MSP-1 protein fragment comprising the p19 fragment (see e.g. page 109, col 1.)"

However column 1 at page 109 refers to the comparison of the cloned C-terminal fragments with other *Plasmodiums* such as *P. vivax*, and *P. falciparum*. There is no mention of the cloning and expression of the *P. cynomolgi* MSP-1 protein fragment comprising the p19 fragment.

There is no information given in Longacre (1995) of how to clone the 19-kDA fragment of any *Plasmodium*.

Furthermore, there is no disclosure in Longacre (1995) that the 19 kDa C-terminal fragment of the MSP-1 is that of SEQ ID NO: 11 and that this particular fragment induces an immune response which can inhibit parasitemia in vivo in a host infected with a *Plasmodium* parasite, as recited in Claim 153 and that exceptional results were achieved.

Moreover, there is no disclosure or suggestion of an oligomer of the recombinant protein of Claim 153 in Longacre (1995). An oligomer can be produced using conventional proein techniques such as glutaraldehyde or it can be produced in the baculovirus systems used as described at the bottom of page 14 of the specification.

Longacre et al (1994) disclose the construction of various recombinantly produced proteins from *Plasmodium vivax* MSP-1 in baculovirus such as analogs of the 42-kDa or 19 kDa C-terminal processing products. Anchored and non-anchored recombinant constructs were made as set forth in Figure 2. There is simply no disclosure in Longacre et al (1994) that these particular recombinant proteins can induce an immune response which can inhibit parasitemia *in vivo* in a host infected with a *Plasmodium* parasite.

Thus, neither Longacre (1995) nor Longacre et al (1994) demonstrate that their particular constructs can inhibit parasitemia *in vivo* in a host infected with a *Plasmodium* parasite. As stated in the Longacre Declaration dated June 16, 2006 in paragraph 4:

> It should be appreciated that without experimentally demonstrating that parasitemia can be reduced or inhibited in vivo in a host infected with a *Plasmodium* parasite infectious to humans, it could not be predicted at that epoch whether these sequences (Longacre 1995) or recombinant proteins Longacre et al (1994) could in fact be useful in a vaccinating composition.

Thus, the mere suggestion in both cited references that the recombinant constructs could potentially or possibly be used as vaccines would not lead the skilled artisan at that period of time to conclude that they are vaccines, which could inhibit parasitemia in a host infected with a *Plasmodium*

Finally, Longacre et al (1994) does not suggest to the skilled artisan to select the p19 MSP-1 recombinant construct for vaccinating purposes and not p42 MSP-1. Indeed a comparison of the results obtained upon vaccination in the toque macaque *Macaca sinica* monkeys showed superior results with p19 in comparison with p42 (Compare Figures 6 D and 6 E). Moreover, with the second challenge with the six immunized monkeys with p19 had no detectable parasitemia except for 1 animal in each group which exhibited parasitemia of 0.008% for 1 day. These results are unexpected in view of the teachings of Longacre (1995) and Longacre et al (1994).

Thus, Applicants submit that Claims 153, 169, 172 and 175 are unobvious in view of the two cited Longacre references. Therefore, withdrawal of this rejection is respectfully requested.

Hence, none of the references when combined disclose or suggest a vaccinating composition against a *Plasmodium* parasite which is infectious in man that inhibits parasitemia in vivo in a host infected with said *Plasmodium* parasite that is infectious in man. This had to be demonstrated, due to the unpredictability in the malaria art at that period of time.

Therefore, in view of the foregoing, withdrawal of this rejection is respectfully requested.

Claims 151, 152, 154, 155, 157, 158, 160, 161, 163, 164, 166, 167, 168, 170, 171, 173 and 174 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Chappel and Holder, Miller et al, Longacre et al (1994) and Longacre (1995). For the following reasons, this rejection is respectfully traversed.

Chappel and Holder disclose monoclonal antibodies that inhibit *Plasmodium falciparum* invasion *in vitro* and recognize the first EGF- like domain of the MSP-1.

The Examiner relies upon this reference as disclosing "a recombinant baculovirus producing a soluble *P. falciparum* MSP-1 protein comprising the p19 fragment EGF-like domains."

However, this construct, S42ΔA contains the C-terminal 271 amino acids from the Wellcome T9-94 MSP1 allele. This construct does not contain only p19 from Asn at amino acid position 3 to Ser at amino acid position 95 of SEQ ID NO:1 nor Asn at amino acid position 3 to Ile at amino acid position 116 of SEQ ID NO: 4. Nor is there any suggestion to modify S42ΔA in Chappel and Holder to a shorter sequence.

Miller et al is cited only to orient the sequences in Chappel and Holder.

Longacre et al (1994) and Longacre (1995) were discussed above and the same arguments are incorporated herein by reference. It should be recalled that neither of these articles describe the superior vaccinating results obtained with MSP-1 p19.

The combination of these references fails to render the claims in this rejection obvious since none of these references disclose a recombinant protein that induces an immune response which can inhibit parasitemia in vivo in a host infected with a *Plasmodium* parasite. The terminology "possible," "probable," and "potential," when referring to the recombinant constructs as vaccines is not an indication that they can induce an immune response which can inhibit parasitemia in vivo in a host infected with a *Plasmodium* parasite. Indeed, as set forth in the Longacre Declaration of record, it was simply not predictable at that period of time whether the cited prior art sequences could be used in a vaccinating composition.

Therefore, in view of the above, withdrawal of this rejection is respectfully requested.

Claims 134, 139 to 142, 148, 150, 176 and 177 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Chappel et al, Miller et al and Longacre (1994) in view of Longacre et al (1995) and further in view of Holder et al. For the following reasons, this rejection is respectfully traversed.

Chappel et al., Miller et al, Longacre (1994) and Longacre et al (1995) were discussed above and the same reasoning applies to this rejection. It should be recalled that the combination of these references fails to render the claims in this rejection obvious since none of these references disclose a recombinant protein that induces an immune response which can inhibit parasitemia in vivo in a host infected with a *Plasmodium* parasite. As set forth in the Longacre Declaration of record, it was simply not predictable at that period of time whether the cited prior art sequences or recombinant proteins could be used in a vaccinating composition.

Holder et al does not remedy the deficiencies of the cited primary references, since this patent also does not disclose or suggest a vaccinating composition against a *Plasmodium* parasite which is infectious in man and inhibits parasitemia in vivo in a host infected with the

Plasmodium parasite. Holder et al only demonstrate that a *P. yoeli* construct can inhibit parasitemia in mice and *P. yoeli* is not infectious in man.

Indeed it was not predictable whether the sequences or recombinant proteins cited in the prior art of record in this rejection could in fact be vaccinating compositions since it was not predictable whether the sequences or recombinant proteins could inhibit parasitemia *in vivo*.

Applicants thus submit that the presently claimed invention is unobvious in view of the cited prior art. Therefore in view of the above, withdrawal of this rejection is therefore respectfully requested.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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